

**AMENDMENTS TO THE DRAWINGS**

The attached 3 sheets of drawings include the formal drawings of Reaction Schemes 1-3. These 3 sheets, labeled as Figures 1-3 amend and replace the informal Reaction Schemes appearing on pages 17 and 20 of the specification as originally filed

Attachments: Formal Drawings for Figures 1-3

### **REMARKS**

Reconsideration of the above-identified application in view of the following remarks is respectfully requested.

#### **I. Status of the Specification**

The specification has been amended at the Examiner's request to remove Reaction Schemes 1, 2, and 3 from the specification and, instead, resubmit these schemes as formal drawings. Accordingly, the specification has been amended to include a section entitled "Brief Description of the Drawings," wherein the Reaction Schemes are cross-referenced to Figures 1, 2, and 3. The specification has also been amended to properly cross reference Figures 1, 2, and 3 in the paragraphs that describe Reaction Schemes 1, 2, and 3.

These amendments have been made for purely formal reasons and do not add new matter.

#### **II. Status of the Drawings**

The attached 3 sheets of drawings include the formal drawings of Reaction Schemes 1, 2, and 3 (Figures 1, 2, and 3 respectively). This amendment has been made at the Examiner's request and for purely formal reasons. This amendment is supported by the specification as originally filed (See specification pages 17 and 20) and does not add new matter.

#### **III. Status Of The Claims**

Claims 36-58, 61-75, 77 and 84-92 are pending in this application, of which claims 36-58, 61, 64-75 and 77 have been withdrawn from consideration. Claims 36, 37, 38, 43, 49, 62, 64, 73, 75, 77, and 91 have been amended by way of this Response

Claims 36, 37, 38, 43, 62, 64, 73, 75, and 77 have been amended as suggested by the Examiner to more accurately convey the identity of the groups  $M^1\text{-NH-}$  and  $M^2\text{-O-}$ . As amended, the claims clarify that the "NH" and "O" are each part of the peptide and oligonucleotide,

respectively, and are not separate moieties. Support for these amendments is found throughout the specification, for example, on page 8, lines 21-24 and one page 11, lines 5-9.

Claims 49 and 91 have been amended to more accurately represent the points of attachment for the phosphorous-containing moieties recited in the claims. Support for these amendments is found throughout the specification, for example, on page 12, lines 4-10 and in the compounds described and synthesized in Example 5a.

The withdrawn claims of Group I (claims 36 and 67-72) are process claims that have been amended to include all of the limitations of the elected product claims of Group VII. The withdrawn claims have been maintained as pending in the application. In accordance with MPEP §821.04 and *In re Ochiai*, 71 F.3d 1565, 37 USPQ 1127 (Fed.Cir.1995) the Examiner is requested to rejoin the withdrawn process claims upon allowance of product claims.

Applicant reserves the right to file one or more divisional or continuation applications directed to any cancelled subject matter or any other subject matter disclosed in the application but not encompassed by the pending claims.

All amendments are supported by the application as originally filed. Accordingly, no new matter has been added by way of this Response.

#### **IV. Species Election Requirement**

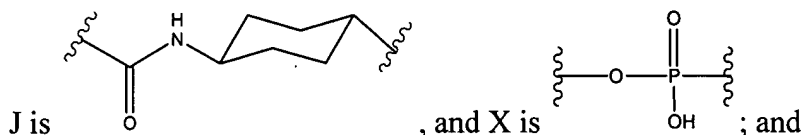
The Examiner has subjected the elected pending claims (Group VII; claims 62, 63, 84-86 and 88-92) to a species election requirement and, thus, requires that we elect a single disclosed species to which the claims will be restricted if no generic claim is finally held to be allowable. The Examiner asserts that the elected claims are directed to the following patentably distinct species in Formula VI:

1.  $M^1$ : a specific peptide residue (or molecule bearing an amino group if so claimed hereafter);
2. A: a specific alkylene or arylene group;

3. D: a specific C<sub>1-4</sub> alkylene or C<sub>3-12</sub> arylene group;
4. B: a specific linker or X-J (specific compounds thereto, as claimed); and
5. M<sup>2</sup>: a specific oligonucleotide.

In order to be fully responsive to the species election requirement, Applicants hereby elect the following species for continued examination, *with traverse*:

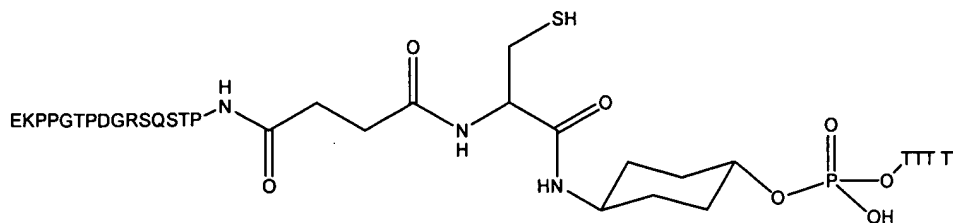
1. M<sup>1</sup>-NH- is a residue of the peptide PTSQSRGDPTGPPKE (substituted at the N-terminus);
2. A is ethylene;
3. D is methylene;
4. B is X-J, wherein



5. M<sup>2</sup>-O- is a residue of the oligonucleotide TTT TT (substituted at the 5' oxygen).

Each of claims 36, 62, 64, 66, 67, 68, and 84-86 and 88-92 read upon the elected species.

The Examiner has also requested that the complete compound with all elected species be drawn out so that there is no confusion as to the elected species. Accordingly, the compound containing the elected species for groups 1-5 has the following chemical structure:



Applicants respectfully traverse the species election requirement as it relates to species election subgroups 1-3 and 5, and reserve the right to file a petition under 37 C.F.R. §1.144.

Applicants submit that a species election requirement is proper only if there is a patentable difference between the each of the claimed species and there would be a serious burden on the Examiner if restriction were not required. Election of species should not be required, however, between claimed species that are not patentably distinct (*See* MPEP 808.01(a)).

The Examiner has required an election of specific moieties for each of Groups 1-5, however, the applicants submit that that the election requirement is not proper for groups 1-3 and 5.

For Group 1: Applicants have chosen a specific peptide residue from Table 3 of the specification. Although the Examples in the specification are sufficiently representative of the claimed methods and resultant compounds, they do not limit the invention or the claims. The invention provides a novel scaffold for the conjugation of, for example, a peptide to an oligonucleotide. The methods of the present invention are of general applicability and are not restricted by the identity of M<sup>1</sup>. Thus, one of skill in the art would recognize that each peptide and molecule bearing an amino group would be interchangeable in the context of the invention, i.e., as the peptide or amino bearing moiety bound to the scaffold.

For Group 2: Applicants have elected ethylene for "A." Applicants submit that all other alkylene species are of similar structure to ethylene because they are homologs of ethylene. The arylene moieties are unsaturated ring-based analogs of the alkylens and serve the same function in the same way. Furthermore, in the context of the present invention, "A" is used as an inert spacer moiety that links two carbonyl functionalities. The carbonyls act to conjugate the peptide and oligonucleotide. Applicants submit the claimed alkylene and arylene species possess similar structural and/or functional properties in the context of the present invention (i.e., they function as unreactive linkers). Thus, one of skill in the art would recognize that, in context, the alkylens and arylens are interchangeable and, therefore, not separately patentable.

For Group 3: Applicants have elected methylene for D. Applicants submit that all other C<sub>1-4</sub> alkylene species are of similar structure to methylene because they are homologs of methylene. The arylene moieties are unsaturated ring-based analogs of the alkylens and serve the same function in the same way. Furthermore, in the context of the present invention, "D" is used as a inert moiety

that links the reactive SH functionality to the remainder of the Formula VI scaffold. Using parallel reasoning to that for Group 2 (*supra*), the species of Group 3 possess similar structural and/or functional properties in the context of the present invention (i.e., they function as unreactive linkers). Thus, one of skill in the art would recognize that each C<sub>1-4</sub> alkylene or C<sub>3-12</sub> arylene are interchangeable and, therefore, not separately patentable.

For Group 5: Applicants have chosen a specific oligonucleotide residue from Table 3 of the specification. Although the Examples in the specification are sufficiently representative of the claimed methods and resultant compounds, they do not limit the invention or the claims. The invention provides a novel scaffold for the conjugation of, for example, a peptide to an oligonucleotide. The methods of the present invention are of general applicability and are not restricted by the identity of M<sup>2</sup>. Thus, one of skill in the art would recognize that each oligonucleotide would be interchangeable in the context of the invention, i.e., as the oligonucleotide bound to the scaffold.

Based on the foregoing remarks it is respectfully submitted that, in the context of the present invention, Groups 1-3 and 5 do not contain patentably distinct species. Accordingly, reconsideration of the species election requirement is respectfully requested.

**CONCLUSION**

In view of the above remarks, this application is believed to be in condition for allowance, which is earnestly solicited.

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Respectfully submitted,

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22

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**FORMAL DRAWINGS**